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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/565,220	05/22/2006	Ogari Pacheco	4705-0118PUS1	9789

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EXAMINER	
HA, JULIE	

ART UNIT	PAPER NUMBER
1654	

NOTIFICATION DATE	DELIVERY MODE
09/18/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/565,220	PACHECO ET AL.	
	Examiner	Art Unit	
	Julie Ha	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 August 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *37-40,42,43,46-59,61,62,64 and 65* is/are pending in the application.

4a) Of the above claim(s) *49-59,61,62 and 64-68* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *37-40, 42-43 and 46-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Amendment after Non-final filed on August 14, 2007 is acknowledged. Claims 41, 44-45, 60 and 63 have been cancelled. Claims 37-40, 42-43, 46-59, 61-62 and 64-65 are pending in this application. Applicant's election of Group I (claims 37-48) with traverse filed on March 27, 2007 is acknowledged. The Restriction is deemed proper and is made FINAL. Claims 49-59, 61-62 and 64-68 are withdrawn from consideration as being drawn to nonelected invention, pursuant to 37 CFE 1.142(b), there being no allowable generic or linking claim. Claims 37-40, 42-43 and 46-48 are examined on the merits in this office action.

Withdrawn Rejection

1. All rejections not cited herein are hereby withdrawn due to Applicants' amendments.

New Ground for Rejection

35 U.S.C. 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 37-40, 42, 43, 46-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lipari et al (US Patent # 6232333).

6. The instant claims are drawn to a pharmaceutical composition for oral administration of saquinavir comprising: 10-80% saquinavir or its pharmaceutical acceptable salts, a long chain fatty acid (20-80% oleic acid), at least an alcohol (2% to 20% ethanol or propylene glycol), a non-ionic surfactant (10% to 20% castor oil or polyoxyethylene sorbitan ester), and a pharmaceutically acceptable antixoxidant (0.1% to 2% tocopherol or butylated hydroxytoluene). The claims are further drawn to the

pharmaceutical composition which is fractionated in single doses in the form of soft gelatin capsules and in the form of hard gelatin capsules.

7. As described in the previous office action, Lipari et al teach a liquid pharmaceutical composition comprising HIV protease providing oral bioavailability. The composition comprises a solution in a pharmaceutically acceptable organic solvent of a) the HIV protease inhibitor and, b) a surfactant, and can be encapsulated in either hard gelatin capsule or soft elastic capsule (SEC) (see abstract) useful for inhibiting an HIV infection and treating AIDS in humans (see column 32, lines 65-67). This reads on claims 46 and 47. Furthermore, the reference teaches that the HIV protease inhibitors as individual compounds are the compound of formula III or V or saquinavir or nelfinavir or indinavir or VX-478 (see column 7, lines 8-11). This reads on claim 37(i). Additionally, the reference teaches a pharmaceutically acceptable organic solvent which comprises a pharmaceutically acceptable long chain fatty acid or a mixture of a pharmaceutically acceptable long chain fatty acid and pharmaceutically acceptable alcohol, and a pharmaceutically acceptable surfactant (see column 7, lines 22-27). This reads on claims 37 (ii), (iii), and (iv). Furthermore, the reference teaches that the solution composition can also comprise an antioxidant (ascorbic acid, BHA, BHT, vitamin E, vitamin E PEG 1000 succinate) for chemical stability (see column 8, lines 8-12). This reads on claim 37 (v). The reference lists the oleic acid as one of the fatty acid (see column 8, line 25), ethanol as one of the acceptable alcohol (see column 8, line 28), and non-ionic surfactants as derivatives of castor oil, Cremophor EL, Cremophor RH 40, and polyoxyethylene sorbitans 20, 40, 60 and 80 (see column 8, lines 35-63). This reads on

claims 37, 39, 40 and 42-43. The reference further teaches that the solubilized HIV protease compound in the amount of from about 1% to about 50% (preferably 1 to 40%, 10 to 40% or 15 to 40%) by weight of the total solution (see column 9, lines 9-17), fatty acid in the amount of from about 20% to about 99% (see column 9, lines 20-21), alcohol in the amount of from about 0 to 15% (see column 9, lines 28-29), surfactant in the amount of from about 0 to 40%, encapsulated in a soft elastic gelatin or a hard gelatin capsule (see column 9, lines 31-36). This further reads on claims 37-40, 42-43 and 46-47. Further, the reference teaches the concentration ranges for ethanol (10%), oleic acid (52.5%), non-ionic surfactants (castor oil, about 1 to 20%, preferably about 5% to about 10%) and antioxidant (0.01 to 0.08%) (see columns 10-12). This further reads on claims 37-40, 42-43 and 46-47. The reference further teaches that the parent drug area under the curve (AUC) was calculated by the trapezoidal method over the time course of the study. The absolute bioavailability of each test composition was calculated by comparing the area under the curve after oral dosing to that obtained from a single intravenous dose (see column 32, lines 36-41). Although the reference is silent as the AUC for saquinavir, since the pharmaceutical composition having saquinavir would have the inherent properties and characteristic, this reads on claim 48. The difference between the reference and the instant claims is that the reference does not teach tocopherol or butylated hydroxytoluene in a concentration ranging from 0.1% to 2% in weight of the final composition.

8. However, it would have been obvious to one of ordinary skill in the art to optimize the conditions of Lipari et al patent '333, and try different concentrations of different HIV

protease inhibitors in combination with components (oleic acid, ethanol, castor oil and tocopherol) to formulate the pharmaceutical composition. There is a reasonable expectation of success, since Lipari et al disclose a finite number of HIV protease inhibitors, and reasonable number of different components that are in the pharmaceutical composition.

9. The MPEP states the following: Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. *"[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation."* *In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955)* (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 (*"The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."*); *In re Hoeschele, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969)* (Claimed elastomeric polyurethanes which fell within the broad scope of the references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.). For more

recent cases applying this principle, see Merck & Co. Inc. v. Biocraft Laboratories Inc., 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989); *In re Kulling*, 897 F.2d 1147, 14 USPQ2d 1056 (Fed. Cir. 1990); and *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997). Therefore, there is a reasonable expectation of success since the Lipari patent teaches the composition of claimed invention reciting a finite number of HIV protease inhibitors (8) and oleic acid, ethanol, castor oil, and butylated hydroxytoluene in a hard gelatin capsules or soft elastic capsules, and "*The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages*"

Rejection-35 U.S.C. § 112, 1st

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 37, 39 and 40 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time of the application was filed, had possession of the claimed invention.

The claims are drawn to a pharmaceutical composition for oral administration of saquinavir comprising: saquinavir (10-80%), oleic acid (20-80%), alcohol or propylene glycol (2-20%), castor oil or polyoxyethylene sorbitan ester (10-20%) and tocopherol or butylated hydroxytoluene (0.1-2%) and wherein oleic acid is employed in a concentration of about 50% in weight of the final composition.

Lack of Ipsis Verbis Support

12. The specification is void of any literal support for the 10% to 20% of castor oil or polyoxyethylene sorbitan ester, 0.1% to 2% of tocopherol or butylated hydroxytoluene, and 50% oleic acid. In the context of 10% to 20% castor oil or polyoxyethylene sorbitan ester, the word "10% to 20%" is not present anywhere in the specification. In Table 1, examples of saquinavir concentrate compositions are disclosed. Saquinavir is in the range of 10.6% to 32%; oleic acid is in the range of 10% to 28%; tocopherol is in the range of 0.19% to 0.4%; castor oil is in the range of 3.6% to 11.97%; ethanol is in the range of 51% to 53%. The range of 10% to 20% of castor oil is not found. The only concentration that is close to 10% to 20% is composition C2 wherein the castor oil concentration is 11.97% (see Table 1, C2). The range of 0.1% to 2% of tocopherol is not found. As described above, the tocopherol concentration range disclosed is 0.19% to 0.4%. This range is near the low limit of 0.1%. There is not enough literal support for the tocopherol range of 0.1% to 2%. Furthermore, the oleic acid claimed in claim 39 is about 50%. Oleic acid is disclosed in the range of 10% to 28% (see Table 1). This falls short of about 50% oleic acid. Furthermore, the specification does not disclose the

ethanol range of 2% to 20%. Table 1 shows that the concentration range of ethanol is from 51% to 53%. The claims recite that saquinavir is in 10-80%, oleic acid in 20-80%, ethanol or propylene glycol in 2-20%, castor oil or polyoxyethylene sorbitan ester in 10-20%, and tocopherol or butylated hydroxytoluene in 0.1-2%. However, the examples shown have saquinavir in 10.6-32%, oleic acid in 10-28%, ethanol or propylene glycol in 51-53%, castor oil or polyoxyethylene sorbitan ester in 3.6-11.97%, tocopherol or butylated hydroxytoluene in 0.19-0.4%. Thus, ethanol, castor oil and oleic acid range in the composition fall outside of the claimed ranges.

Lack of Implicit or Inherent Support

13. "While there is not in *haec verba* requirement, newly added claim limitations must be supported in the specification through express, implicit, or inherent disclosure." See MPEP 2163. Thus support can be furnished implicitly or inherently for a specifically claimed limitation. However, the specification lacks any implicit or inherent support for the claimed "10%-20% castor oil", "0.1% to 2% tocopherol" and "50% oleic acid". As explained supra, there is no support for any concept of"10%-20% castor oil", "0.1% to 2% tocopherol" and "50% oleic acid in the specification. Additionally, the ethanol range falls outside of the claimed range of 2% to 20%. Additionally, the examples given (e.g., Example 6) also do not calculate to the final concentration of the each of the components claimed. Example 6 discloses that 600 g (60%) of saquinavir and 3000 mL of absolute ethanol are added. The calculation gives about 17% concentrated composition. The solution is filtered and to the filtrate, oleic acid (200 g-20%) and the

tocopherol (7.44 g-0.744%) are added. This would give approximately 16% saquinavir concentration, 5.3% oleic acid, and 0.2% tocopherol concentration, respectively, assuming all 3000 mL of the liquid remained in the filtrate. The mixture was concentrated and to this, 150 g of castor oil is added. Thus, the % calculated at the end does not correspond to the concentration ranges claimed in the instant application.

Conclusion

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).. No claims are allowed.

15. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Julie Ha whose telephone number is 571-272-5982. The examiner can normally be reached on Mon-Fri, 8:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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